

**AMENDMENT TO THE CLAIMS**

This listing of claims will replace all prior listings of claims in the application.

1. (Withdrawn) A method for treating diabetes mellitus in an individual in need thereof, said method comprising:

administering to said individual a composition providing a gastrin/CCK receptor ligand and an EGF receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells.

2. (Withdrawn) The method of Claim 1, wherein said EGF receptor ligand is an EGF receptor ligand is selected from the group consisting of EGF1-53, EGF1-48, or EGF1-47 congener of EGF1-48, and an EGF1-49 congener of EGF1-48.

3. (Withdrawn) The method of Claim 2, wherein said EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 congener is human EGF1-53, EGF1-48, or its EGF1-47 or EGF1-49 or its congener.

Claims 4-18. (cancelled)

19. (Withdrawn) The method of Claims 1, wherein said gastrin/CCK receptor ligand is a gastrin.

20. (Withdrawn) Pancreatic islet precursor cells treated *ex vivo* with a sufficient amount of gastrin/CCK receptor ligand and an EGF receptor ligand to induce proliferation of said pancreatic precursor islet precursor cells into mature insulin-secreting  $\beta$ -cells, whereby an expanded population of said mature insulin-secreting  $\beta$ -cells is obtained.

21. (Withdrawn) A method for obtaining an expanded population of insulin-secreting  $\beta$ -cells, said method comprising:

providing pancreatic islet precursor cells with a sufficient amount of gastrin/CCK receptor ligand and an EGF receptor ligand to induce proliferation of said insulin-secreting  $\beta$ -cells, whereby said insulin-secreting population of pancreatic  $\beta$ -cells is obtained.

22. (Withdrawn) The method of Claim 21, wherein said providing is *ex vivo*.

23. (Withdrawn) A method for treating diabetes mellitus in an individual in need thereof; said method comprising:

administering to said individual:

a composition providing a gastrin/CCK receptor ligand selected from the group consisting of gastrin and cholecystokinin; and

an EGF receptor ligand selected from the group consisting of EGF1-53, EGF1-48, or its EGF1-47 congener of EGF1-48, and an EGF1-49 congener of EGF1-48;

in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells.

24. (Withdrawn) A method for obtaining an expanded populations of insulin-secreting pancreatic  $\beta$ -cells *ex vivo*, said method comprising:

providing pancreatic islet precursor cells with a sufficient amount of;  
a composition providing a gastrin/CCK receptor ligand selected from the group consisting of gastrin and cholecystokinin; and

a EGF receptor ligand selected from the group consisting of TGF- $\alpha$ , EGF1-53, EGF1-48, or its EGF1-47 congener of EGF1-48, and an EGF1-49 congener of EGF1-48;

whereby said insulin-secreting population of pancreatic  $\beta$ -cells is obtained.

Claims 25-27. (cancelled)

28. (Withdrawn) The method according to Claims 21 or 24, wherein said precursor cells are obtained from a donor.

29. (Withdrawn) The method according to Claim 28, wherein said donor is a cadaver.

Claims 30-38. (Cancelled)

39. (Withdrawn) A method for treating diabetes mellitus in an individual in need thereof, said method comprising:

administering to said individual a composition providing a gastrin/CCK receptor ligand and an EGF receptor ligand in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells, wherein said gastrin/CCK receptor ligand is a gastrin and said EGF receptor ligand is EGF 1-53.

40. (Withdrawn) A method for obtaining an expanded population of insulin-secreting pancreatic  $\beta$ -cells, said method comprising:

providing pancreatic islet precursor cells with a sufficient amount of gastrin/CCK receptor ligand and an EGF receptor ligand to induce proliferation of said insulin secreting pancreatic  $\beta$ -cells, wherein said gastrin/CCK receptor ligand is gastrin and said EGF receptor ligand is EGF 1-53, whereby said insulin-secreting population of pancreatic  $\beta$ -cells is obtained.

41. (Withdrawn) A method for treating diabetes mellitus in an individual in need thereof, said method comprising:

administering to said individual:

a composition providing a gastrin/CCK receptor ligand. Wherein said gastrin/CCK receptor ligand is a gastrin; and

an EGF receptor ligand, wherein said EGF receptor ligand is EGF 1-53;

in an amount sufficient to effect differentiation of pancreatic islet precursors cells to mature insulin-secreting cells.

42. (Withdrawn) A method for obtaining an expanded population of insulin-secreting pancreatic  $\beta$ -cells *ex vivo*, said method comprising:

providing pancreatic islet precursor cells with a sufficient amount of;  
a composition providing a gastrin/CCK receptor ligand, wherein said gastrin/CCK receptor ligand is a gastrin; and

an EGF receptor, wherein said EGF receptor ligand is EGF 1-53;

whereby said insulin-secreting population of pancreatic  $\beta$ -cells is obtained.

43. (Withdrawn) Pancreatic islet precursor cells treated *ex vivo* with a sufficient amount of a gastrin/CCK receptor ligand and an EGF receptor ligand to induce proliferation of said pancreatic islet precursor cells into mature insulin-secreting  $\beta$ -cells, whereby an expanded population of said mature insulin-secreting  $\beta$ -cells is obtained, wherein said gastrin/CCK receptor ligand is a gastrin and sad EGF receptor ligand is EGF 1-53.

44. (Previously Presented) A kit comprising in a container

as a first component a therapeutically effective amount of a sterile gastrin/CCK receptor ligand and

as a second component a therapeutically effective amount of a sterile EGF receptor ligand,

wherein said gastrin/CCK receptor ligand is a gastrin and said EGF receptor ligand is EGF 1-53 for administration separately or in combination to a patient, and

wherein said gastrin/CCK receptor ligand and said EGF receptor ligand in said kit are suitable for inclusion in a pharmaceutical composition for administration to a human patient.

45. (Previously Presented) A kit according to claim 44 wherein the therapeutically effective amount of the first component and the therapeutically effective amount of the second component are sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells in the patient.

46. (Previously Presented) A kit according to claim 44 wherein the first and second component are included in a single container.

47. (Previously Presented) A kit according to claim 44 wherein the first component and second component are in a sterile aqueous buffer.

48. (Previously Presented) A kit according to claim 44 wherein the first component and second component are in the form of a dry lyophilized powder or water free concentrate.

49. (Previously Presented) A kit according to claim 48 further comprising sterile water for reconstituting the first component and second component.

50. (Previously Presented) A kit according to claim 44 further comprising a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products which notice reflects approval by the agency for manufacture, use or sale of the kit for human administration.

51. (Previously Presented) A kit according to claim 50 wherein the notice reflects approval by the regulatory agency for manufacture, use or sale of the kit for administration to a human to treat diabetes.

52. (Previously Presented) A kit comprising in a container

a therapeutically effective amount of a sterile gastrin/CCK receptor ligand suitable for preparing a pharmaceutical composition suitable for administration to a human patient; and

a therapeutically effective amount of a sterile EGF receptor ligand suitable for preparing a pharmaceutical composition suitable for administration to a human patient,

wherein said gastrin/CCK receptor ligand is a gastrin and said EGF receptor ligand is EGF 1-53, and one or more pharmaceutically acceptable carrier or excipient capable of forming said pharmaceutical composition.

53. (Previously Presented) A kit according to claim 52 wherein the gastrin/CCK receptor ligand and EGF receptor ligand are in a sterile aqueous buffer.

54. (Previously Presented) A kit according to claim 52 wherein the gastrin/CCK receptor ligand and EGF receptor ligand are in the form of a dry lyophilized powder or water free concentrate.

55. (Previously Presented) A kit according to claim 54 further comprising sterile water for reconstituting the gastrin/CCK receptor ligand and EGF receptor ligand.

56. (Previously Presented) A kit according to claim 52 wherein the therapeutically effective amount of sterile gastrin/CCK receptor ligand and therapeutically effective amount of a sterile EGF receptor ligand are sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells in a patient.

57.-58. (Cancelled)